





Supplementary Material

Biomarkers and detection techniques for genotoxic damage in workers exposed to benzene, toluene, and xylene: a narrative review

Biomarcadores y técnicas de detección de daño genotóxico en trabajadores expuestos al benceno, tolueno y xileno: una revisión narrativa

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ANNEX 1



Annex 1. Table summarizing the selected articles and references

Main author	Year	Methodology	Target	Main results
Sisto R	2019	Analytical, experimental, cross-sectional study	To determine circulating MicroRNAs as a potential biomarker of occupational exposure to low doses of organic solvents.	Two miRNAs (miRNA 6819-5p and miRNA 6778-5p) related to oxidative stress were identified significantly in subjects exposed mainly to Xylene.
Moor AM	2019	Analytical, experimental, cross-sectional, experimental study	Evaluation of immunological, inflammatory and oxidative stress biomarkers in workers exposed to BTX.	There was decreased expression of CD80 and CD86 in the exposed groups, elevated cytokine levels and decreased IL-10.
Londoño-Velasco	2019	Analytical, experimental, cross-sectional, experimental study	To determine the effects of occupational exposure to organic solvents and paints on oxidative and DNA methylation damage in painters.	Exposed painters had significantly higher levels of oxidative DNA damage and alterations in methylation patterns compared to the control group, suggesting an increased risk of genotoxic effects associated with occupational exposure.
Palma M	2015	Descriptive cross-sectional study	To evaluate exposure to organic solvents in car painters in Bogotá and its effects on health.	Elevated levels of solvent metabolites in urine were found in the exposed group, with positive correlations between the environmental concentration of toluene and xylene and their metabolites. Some workers exceeded permissible exposure limits.
Sisto R	2020	Analytical, experimental, cross-sectional, experimental study	Comparing biomarkers of oxidative stress and DNA damage in painters with occupational exposure to volatile organic compounds.	Significant associations were found between DNA damage, 8-oxoguo and methylhippuric acid concentrations.
Lagorio S	1994	Analytical, experimental, cross-sectional, experimental study	To evaluate the association between 8-OHdG excretion and the level of exposure to benzene and other aromatic compounds among exposed individuals.	High levels of exposure were identified in the group, and a significant relationship was identified between urinary 8 OHdG and benzene exposure.
Kim JH	2021	Analytical, experimental, cross-sectional, experimental study	To evaluate changes in stress biomarkers and gene expressions in workers exposed to volatile organic compounds.	ENO3, CDNA FLJ39461 expressions were significantly associated with increased MDA, specifically to toluene exposure.

Inoue O	2000	Analytical, experimental, cross-sectional, experimental study	Proposes PMA measurement as a biomarker of occupational exposure to benzene.	PMA was identified as a marker of benzene exposure over other metabolites. No PMA was detected in the urine of unexposed individuals.
Xiong F	2016	Analytical, experimental, cross-sectional, experimental study	Determine airborne BTEX levels in offices and fueling areas of gas stations.	Higher levels of occupational exposure to T-SOD and GSH activities were significantly reduced in those exposed. Additionally, MDA and 8-OHdG, and micronuclei were elevated in those exposed.
Cardenas Bustamante O	2007	Analytical, experimental, cross-sectional, experimental study	Investigate exposure to organic solvents and genotoxic effects by cytogenetic monitoring.	None of the biomarkers of early genetic effects in the participating workers were found to be above baseline values
Villalba-Campos M	2016	Analytical, experimental, cross-sectional, experimental study	To evaluate the genotoxic effect of occupational exposure to aromatic hydrocarbons used as solvents and paint strippers.	The most frequent chromosomal alterations were fragilities, followed by chromosomal breaks and chromatid breaks.
Salem E	2018	Analytical, experimental, cross-sectional, experimental study	To investigate genotoxicity due to occupational exposure to benzene in gasoline station workers.	Higher levels of DNA fragmentation optical density and higher percentages of dead cells were identified within the exposed group.
Sha Y	2014	Analytical, experimental, cross-sectional study	Evaluate and compare hematological parameters mRNA expressions of PARP1, PARG and PARP activity and mRNA expressions of DNA methyl transferases (DMT).	PARP1 mRNA expression decreased in the exposed groups. Expression of DNMT and MBD2 as DNA methylation status showed that DNA methyltransferases were downregulated.
Holz O	1995	Analytical, experimental, cross-sectional, experimental study	To determine cytogenetic effects in employees of a styrene production plant exposed to aromatic hydrocarbons.	Higher urinary metabolites of sirene, ethylbenzene and benzene. The frequency of MN was not as significantly high.



Santiago F	2017	Analytical, experimental, cross-sectional, experimental study	To characterize the cytogenetic, hematological and immunophenotypic status in 3 women attending a gas station.	Chromosomal rearrangement, decreased NK cells, with abnormal CD1 expression and early miscarriage were found.
Santiago F	2014	Analytical, experimental, cross-sectional study	To describe cytogenetic changes in chromosomes 1,2 and 4 in gas station workers with BTX exposure.	Translocations were the most frequently observed chromosomal aberrations.
Olivero J	2013	Analytical, experimental, cross-sectional, experimental study	Characterize different Thinner samples and to establish a relationship between the type of Thinner and the risk associated with the toxic effects that may occur after exposure.	Many of the components in the samples analyzed were of particular toxicological relevance due to their negative effects on the central nervous system.
Haro-Garcia L	2008	Narrative review	To characterize the association between occupational exposure to benzene, toluene and xylene and hematological manifestations described in the literature.	The identification of biomarkers is limited because it evaluates recent exposure.
Santos M	2013	Observational, cross-sectional study	Assessing the health risk of benzene exposure in a community affected by a fuel leak.	Unsafe exposure to benzene for several months, at levels implying a total cancer risk of 110 to 200 per 10e6 individuals.
Pajaro-Castro	2014	Analytical, experimental, cross-sectional, experimental study	To examine the release of volatile organic compounds from commercially made polystyrene products and discuss their likely impact on human health.	Products based on expanded polystyrene release different chemical substances when heated, these substances can migrate into food and, as a consequence, their use may present some risks to human health.
Gallego-Díez M	2016	Analytical, experimental, cross-sectional, experimental study	Show validation of methods for quantification of BTEX compounds adsorbed on activated carbon.	Demonstrates the test as useful, precise and accurate in recoveries for all analytes.
Source A	2013	Analytical study, experimental cross-sectional study.	To compare the hearing ability related to the central auditory system and peripheral auditory system between solvent-exposed and non-exposed workers.	Solvent-exposed subjects had significantly worse hearing thresholds in the right ear than non-exposed subjects.

Aquinas TD	2016	Analytical, experimental, cross-sectional, experimental study	To evaluate the potential for DNA damage and cytotoxicity in pathology laboratory technicians with occupational exposure to organic solvents.	More DNA damage was identified in the exposed workers group in relation to the control group, according to the comet assay.
Haines D	2017	Analytical cross-sectional study	Determination of solvent levels	Due to random sampling of urine and blood provided biomonitoring data for the general Canadian population.
Cakmak S	2020	Analytical cross-sectional study	Identification of hematological and biochemical effects of exposure to organic solvents.	Higher concentrations of VOCs were evidenced in older age groups, men and hematological alterations such as increased hemoglobin levels.
Rana I	2021	Systematic review and meta-analysis of studies	Relationship between Benzene and non-Hodgkin's lymphoma	Benzene can induce non-Hodgkin's lymphoma at high concentrations.
Aragonese N	2008	Comparative study	Evidence of environmental monitoring based on biomarkers of genotoxic damage.	It is proposed to estimate a surveillance program based on biological samples.
Schanatter R	2020	Qualitative study	Association between Benzene levels and genotoxicity	The studies demonstrated genotoxicity at concentrations of 2 ppm
Laffon B	2013	Analytical cross-sectional study	Effects on workers near oil companies	The exposed people obtained alterations in biomarkers of effect in different systems such as endocrine, immune, nervous, and immune systems.
Alses M	2021	Analytical study of cross-sectional	Determination of hepatotoxicity and oxidative stress effects due to exposure in gas stations.	Exposure to VOCs mainly influences increased hemoglobin counts.
McNally K	2017	Analytical cross-sectional study	Association between metabolite production and benzene exposure	Metabolites increase with smoking and gender and cannot be studied at low exposure.
Sisto R	2020	Analytical cross-sectional study	Evaluation of the microRNA profile as a biomarker of VOC exposure.	An association was found between the expression of 8-oxo-dGuo, a biomarker of oxidative DNA damage with the exposure
MV Crowns	2009	Analytical cross-sectional study	Genetic biomonitoring in the oil industry	Exposed individuals showed DNA damage, and the comet assay was sensitive for detecting damage in this population
Decharat S	2014	Analytical cross-sectional study	Determination of main symptoms of toluene exposure	Neurological symptoms were correlated with high levels of toluene.



Khoury C	2018	Topic review	Standardization of human biomonitoring for some chemical substances.	From the Canadian survey, 50 biomarkers for VOC exposure were developed.
Amoatey P	2018	Critical review	Air pollution and its influence on health problems	Air pollution causes cardiorespiratory problems and cancer, so strategies are being considered.
Huang L	2021	Analytical cross-sectional study	Relationship with Toluene and Benzene exposure and health effect.	High concentrations of Naphthalene, followed by Toluene and Benzene were evidenced in kitchen workers related to oxidative stress.
Andersen ME	2021	Topic review	Physiological variation in alterations of biomarkers of VOC exposure.	Associations have been identified between health outcomes and biomarker concentrations at very low levels of exposure
Crout F	2002	Analytical cross-sectional study	Expression of stress proteins as a test of VOC cytotoxicity.	VOC toxicity generates increased GRP78 expression in all lines, however, it is not considered as a sensitive biomarker.
Kim S	2021	Prospective cohort study	To determine the association of cancer incidence with higher concentrations of toluene.	Toluene concentrations were higher in women, overweight and thyroid cancer; it was not associated with incidence of other cancers.
Rodriguez-Padilla C	2020	Bibliographic review	Alterations due to exposure to low doses of toluene.	Although toluene is not considered a carcinogen, it can cause neurological and hematological disorders.
Zubizarreta S	2018	Bibliographic review	Evidencing the harmful effects of occupational exposure to VOCs	The main effects of exposure to VOCs are on the reproductive system, cardiovascular system and altered DNA repair.

*BTEX: Benzene, Toluene, Ethylbenzene, Ethylbenzene and Xylene, *8-oxodGuo: 8-oxo-7,8-dihydro-2'-deoxyguanosine, *GST: glutathione transferase enzyme, *COV: Xylene, Ethylbenzene, Styrene, Toluene, *MDA: malondialdehyde. Table prepared by the authors.